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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/649,857	08/28/2003	Craig A. Rosen	PZ005P1C3	7386

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EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 09/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/649,857	ROSEN ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/19/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

SDO

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group 35 (original claims 11, 12, 16) on 8/19/05 is acknowledged.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-24 have been canceled and new claims 25-45 (8/19/2005) have been added. New claims 25-45 are drawn to the isolated polypeptide comprising the amino acid sequence of SEQ ID NO:45, which is the same invention encompassed by new claims 25-45.

Claims 25-45 are pending and are under consideration by the Examiner.

Specification

2. According to the priority statement of 8/28/2003, it appears that priority is being claimed to a large number of provisional applications. These applications appear to be drawn to unrelated subject matter and are either not available for consideration or for which consideration to determine support for the instantly claimed subject matter would require an undue burden. Accordingly, the subject matter defined in claims 25-45 has an effective filing date of 4/7/1998, that of PCT/US98/06801.

Applicants are requested to provide the serial number and specific page numbers of any parent application to which priority is desired which specifically supports the

particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession and fully enabled prior to 4/7/1998.

Claim rejections-35 U.S.C. 101

3. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 25-45 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are directed to an isolated polypeptide 67 amino acids in length. The invention encompassed by this claim has no apparent or disclosed patentable utility. This rejection is consistent with the current utility guidelines, published on 1/5/01, 66 FR 1092. The instant application has provided a description of an isolated protein, but does not disclose a specific and substantial biological role of this protein or its significance. There is no biological activity, phenotype, disease or condition, ligand, binding partner, or any other specific feature that is disclosed as being associated with the mature polypeptide. The mere identification of the polypeptide is not sufficient to impart any particular utility to the claimed polypeptide without any information as to the specific properties of the polypeptide. Since significant further research would be required of a person skilled in the art to determine how the claimed polypeptide is involved in any activities, the asserted utilities are not substantial.

Furthermore, since the asserted utility is not present in a ready-to-use, real-world application, the asserted utility is not substantial.

The specification asserts the following as utilities for the claimed polypeptide of amino acid sequence set forth in SEQ ID NO:45 (see pages 26-28 of the specification):

1. to produce antibodies against the polypeptides;

2. to produce reagents for differential identification of the tissue or cell type present in a biological sample;

3. to use in the treatment of breast cancer and growth disorders;

4. to isolate cognate ligands or receptors;

5. as a diagnostic agent for disease.

Each of these shall be addressed in turn.

1. *to produce antibodies against the polypeptides.*

This asserted utility is not specific or substantial. Since antibodies can be made to any polypeptide, the asserted utility is not specific to the claimed polynucleotide encoding the polypeptide. Furthermore, the specification does not disclose how the antibodies can be used, and therefore further significant research would be required on one skilled in the art to determine how to use the claimed antibodies. Since the asserted utility is not presented in a ready-to-use, real-world application, the asserted utility is not substantial.

2. *to produce reagents for differential identification of the tissue or cell type present in a biological sample.*

The employment of a protein of the instant invention as a tissue specific marker is not a substantial or specific utility since breast specific proteins were already known in the art. All human proteins can invariably be classified into two categories, those which are expressed in a tissue or developmentally specific manner and those which are expressed ubiquitously. It can be alleged that any protein which is expressed in a tissue specific manner can be employed to detect the tissue in which it is expressed in a sample. Alternately, a human protein which is expressed ubiquitously can be employed to detect the presence of any human tissue in a sample. Such utilities are analogous to the assertion that a particular protein can be employed as a molecular weight marker, which is neither a specific or substantial utility.

3. *to use in the treatment of breast cancer and growth disorders.*

This asserted utility is not specific or substantial. The specification alleges that the polypeptides of the instant invention can be used as a putative therapy for various disorders, based on tissue distribution. The specification does not disclose any specific disorders that are associated with altered protein levels or functioning. The specification asserts on page 27, lines 24-37; page 28, lines 1-5) that:

"The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis or treatment of breast cancer and growth disorders. The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify

agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological activities. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytoklnes; immunostimulating/immunosuppressant activities (e.g. for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy; regulation of hematopoiesis (e.g. for treating anaemia or as adjunct to chemotherapy; stimulation or growth of bone, cartilage, tendons, ligaments and/or nerves (e.g. for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g. for treating infections, tumors; hemostatic or thrombolytic activity (e.g. for treating haemopïlia, cardiac infarction etc.); anti-inflammatory activity (e.g. for treating septic shock, Crohn's disease; as antirnicrobials; for treating psoriasis or other hyperproliferative diseases; for regulation of metabolism, and behaviour.

However, the specification merely recites typical biological activities of cytokines in general and does not provide any evidence of a single biological property of the instant protein. Therefore, since the asserted utility is not presented in a ready-to-use, real-world application, the asserted utility is not substantial.

4. *to isolate cognate ligands or receptors.*

This asserted utility is not specific or substantial. There is no experimental evidence presented in the specification with respect to a receptor for the claimed protein and this assertion is, neither convincing nor specific. The specification also does not disclose the presence and/or tissue distribution of a receptor for the protein, and therefore the cell types and tissues that are responsive to the protein *in vivo* are unknown. Since the

asserted utility is not presented in a ready-to-use, real-world application, the asserted utility is not substantial.

5. *as a diagnostic agent for disease.*

The asserted utility is not specific or substantial. The specification does not disclose any specific diseases or disorders associated with expression of the protein. The specification asserts that the gene encoding the protein is primarily expressed in breast cancer and therefore the polypeptide of the instant invention can be used in diagnosis of breast cancer (page 27, lines 10-11; page 27, lines 26-29). However, the specification fails to disclose differential expression of the instant protein in normal breast tissue and in breast cancer tissue. Furthermore, since many polypeptides can and are used as diagnostic reagents, the asserted utility is not specific to the claimed polypeptide. Since the asserted utility is not presented in a ready-to-use, real-world. application, the asserted utility is not substantial.

Claim rejections-35 USC § 112, first paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-45 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantially asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would

not know how to use the claimed invention. The instant specification does not disclose a biological activity for the claimed polypeptide, therefore, there is no specific and substantial asserted utility or well established for the claimed polypeptide.

Claim rejections, 35 U.S.C. § 112, first paragraph

5a. Claims 25, 33, 41, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make use the invention.

The deposit of biological material is considered by the Examiner to be necessary for the enablement of the current invention because the claims require availability of the deposit. Elements required for practicing a claimed invention must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. When biological material is required to practice an invention, and if it is not so obtainable or available, the enablement requirements of 35 USC §112, first paragraph, may be satisfied by a deposit of the material. See 37 CFR 1.802.

The specification does not provide a repeatable method for obtaining ATCC Deposit No. 209074 and it does not appear to be a readily available material. The ATCC® deposit in full compliance with 37 CFR §§ 1.803-1.809 would satisfy the requirements of 35 USC §112, first paragraph.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty

and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or Declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803-1.809 for additional explanation of these requirements.

5b. Claims 41-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated polypeptide at least 90% identical with a particular disclosed sequence (SEQ ID NO:45). The claims do not require that the polypeptide possess any particular conserved structure, function or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved for the biological activity of the protein. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics and structure/function relationship, the specification does not provide adequate written description of the claimed genus.

Vas-cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the ad that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the written

description' inquiry, whatever is *now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she) invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF'S were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Therefore, only a polypeptide of amino acid sequence set forth in SEQ ID NO:45, but not the full breadth of the claims meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

5c. Claims 41-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide of amino acid sequence set forth in SEQ ID NO:45, does not reasonably provide enablement for an isolated polypeptide at least 90% identical to a polypeptide with a particular disclosed sequence

(SEQ ID NO:45). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claim 41, is overly broad in its limitation of "at least 90% identical" because no guidance is provided as to which of the myriad of polypeptide molecules encompassed by the claims will retains the characteristics of the desired polypeptide. Variants of a nucleic acid can be generated by deletions, insertions, and substitutions of nucleotides, but no actual or prophetic examples on expected performance parameters of any of the possible variants of the claimed nucleic acid molecule or muteins of the protein molecule have been disclosed. Furthermore, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia,

causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the instant specification as to how one of skill in the art would generate and use a nucleic acid encoding a polypeptide having at least 80%, amino acid sequence identity with SEQ ID NO:45, other than the polypeptide of SEQ ID NO:45 exemplified in the specification. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Given the breadth of the claims, in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Conclusion

Claims 25-45 are rejected.

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (571) 272-0829.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz

Prema Mertz Ph.D.
Primary Examiner
Art Unit 1646
September 18, 2005